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13. ABSTRACT (Maximum 200 Words) Epidemiological and animal studies associate high levels of dietary fat with increased risk of sex hormone mediated cancer, such as breast cancer. A high intake of total fat and omega-6 fatty acids increases risk while omega-3 (n3) fatty acids are associated with risk reduction. Our proposal is testing the effect of dietary fat and fatty acids on sex hormone concentrations in post-menopausal women. The objectives are to evaluate 1) the effects of total fat and n3 intake on plasma and urinary sex hormone levels, 2) the relationship between plasma fatty acids and plasma and urinary sex hormones, and 3) the effects of total fat and n3 on the association between sex hormone concentrations and urinary prostaglandin E ₂ (PGE ₂). We are performing a randomized, Latin square-designed controlled feeding study testing High Fat, Low Fat, and Low Fat + n3 diets, each of 8 week duration. In order to determine the estrogenic effects of the diets, sex hormone endpoints will be measured reflecting availability, metabolism, and action. Plasma fatty acids fractions and urinary PGE ₂ will be measured to evaluate mechanistic effects. At present 14 women have been screened and 5 are currently enrolled in the trial. No data has yet been generated.							
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Introduction

Our project addresses important questions about the effects of dietary total fat and fatty acids on sex hormone concentrations in postmenopausal women. The study is being conducted at the General Clinical Research Center of the University of Minnesota. Our guiding hypothesis is that dietary total fat and fatty acid content affect sex hormone concentrations in a manner associated with sex hormone mediated cancer risk. The specific objectives are 1) to evaluate the effects of total fat and omega-3 fatty acid intake on plasma and urinary sex hormone levels in postmenopausal women, 2) to evaluate the relationship between plasma concentrations of specific fatty acids and concentrations of plasma and urinary sex hormones, and 3) to evaluate the effects of total fat and omega-3 fatty acids on the association between sex hormone concentrations and urinary prostaglandin E₂ and thromboxane B₂ concentrations.

We are conducting a well controlled feeding study to evaluate the role of fat and fatty acids in 24 healthy, postmenopausal women. The diets being tested include a "high risk" American diet (40% fat), a low fat diet (20% fat) and a low fat diet with supplemental omega-3 fatty acids (23% fat). Endpoints are being measured to assess availability, metabolism, and action of sex hormones in response to the diets. Plasma fatty acids fractions and urinary prostaglandin E₂ is being measured to evaluate mechanistic effects of dietary fat.

Increased understanding of the mechanisms by which dietary fat affect sex hormone action may provide critical information for the development of cancer-preventative dietary recommendations. Nutrition information provided as focused guidelines regarding fat intake can be developed for public use that indicate which types of foods to include in the daily diet and which to avoid.

Body

Study Progress:

The project is proceeding along the time line as defined in our statement of work. Although notification of recommendation for funding was received

Final approval for initiation of the project was received from the Donna S. Ferrandino, PhD, Human Subjects Protection Scientist on 10/15/2004 to submit our revised consent form to the local (University of Minnesota) IRB for approval. Final approval to initiate the project was then received from the University of Minnesota Human Subject Protection Program/Internal Review Board on 10/29/2004.

In order to meet final approval, the development of the diets for the intervention and nutrient calculations of the test diets were complete. Once final approval was secured, work was initiated to develop the food production procedures and coordinate the study needs within the General Clinical Research Center at the University of Minnesota.

Extensive recruitment efforts were initiated as soon as final approval was obtained. We have advertised by placing fliers throughout the medical campus and surrounding campus buildings. A text ad was placed in the Fairview University Medical Center staff and patient flier. To date 14 subjects have been screened by telephone, 6 subjects have been screened at the research

center and 5 subjects are currently participating in the feeding trial. Due to the large time commitment of the trial, careful screening is performed to reduce the possibility of drop-outs from the trial.

Presently no data are available for evaluation. It is our intention to analyze the samples in batches of 4 subjects as they complete the feeding trial. Completion of the feeding phase of the study will take 40 weeks (3-8 week diets with 2-8 week wash-out periods between diets).

Personnel:

The following personnel are presently supported on this grant
Susan Raatz PhD RD, Principle Investigator (5% effort)
Mindy Kurzer PhD, Co-investigator (5% effort)
J Bruce Redmon MD, Co-investigator (5% effort)
Michael Walcher, Senior Scientist (25% effort)
Krista Lundquist, Student Food Service Worker (50% effort)
Shanna Miller, Student Food Service Worker (25% effort)

Key Research Accomplishments

Presently no data are available for evaluation. It is our intention to analyze the samples in batches of 4 subjects as they complete the feeding trial. Completion of the feeding phase of the study will take 40 weeks (3-8 week diets with 2-8 week wash-out periods between diets).

Reportable Outcomes

Training:

This project was included as a rotation project for the Minnesota Consortium for Complementary and Alternative Medicine (CAM) Clinical Research predoctoral Summer Internship from May through August 2004, Michael Croy, RD MS, a graduate student in Human Nutrition worked on the developmental phase of the dietary component of the study.

Lindsay Orr, BA is the current Graduate Research Assistant working on the project. She is a doctoral student in Human Nutrition and is currently funded from a University of Minnesota Graduate School Fellowship. She will be funded by this project in the fall. Lindsay has been performing coordination duties for this trial.

Conclusions

The study is progressing as projected on the "Statement of Work". Given the nature of a long term feeding trial, no reportable data has yet been obtained. The study progress is as expected with recruitment of participants proceeding smoothly. The test diets are well accepted by the participants, all endpoint visits have gone well. We anticipate completion of the first wave of 5 subjects by the fall.

References

None

Appendices

Appendix 1: Diets for Intervention (Statement of Work Task 1)

Sample Menu 2000 Kcal - Day 1

	Menu	High Fat	Low Fat	Low Fat + Omega 3
Breakfast	Grapefruit Juice	130g	200 g	200 g
	Cheerios w/ Sugar	40g 0g	32g 6g	35g 6g
	Bran Muffin w/ Butter	75g (High Fat) 10g	60g (Low Fat) 4g	60g (Low Fat) 4g
	Skim Milk	240g	250g	230g
Lunch:	Turkey Sandwich			
	Whole Wheat Bread	60g	60g	60g
	Turkey Breast	70g	55g	45g
	Butter	6g	0	5g
	Mayonnaise, Regular	10g	6g	0g
	Miracle Whip	0	10g (Fat Free)	10g (Fat Free)
	Egg yolk	2g	5g	4 g
	Flax oil	0g	0	3g
	Lettuce	20 g	20 g	20 g
	Tomato	50 g	50 g	50 g
	Pretzels	0	25g	0
	Potato Chips	35g	0	0
	Applesauce	140g	180g	200g
Dinner:	Orange Roughy	140g	90g	0
	Baked Salmon w/Cajun Spice/Lemon Juice	0 Dash/5g	0 Dash/5g	75g Dash/5g
	White Rice	140g	110g	110g
	Broccoli	80g	80g	80g
	Lettuce/Carrot Salad	50g/15g	50g/15g	50g/15g
	Fat Free French Dressing w/Corn Oil	15g 7g	20g 5g	15g 0
	w/Flax Oil	0	0	5g
	Whole Wheat Bread w/Butter	26g 6g	40g 6g	40g 0
	Angel Food Cake w/Strawberries/Sugar	0 120g/0	50g 120g/6g	50g 120g/6g 0
	Wheat Thins	10g	20g (Regular)	30g (Reduced Fat)
	Mozzarella Cheese	0	30g	40g
	Cheddar Cheese	20g	0	0
	Gumdrops	0	30g	15g
	Grape Juice	0	120g	0

Nutrient Composition (Calculated)

Kcal	2020	2011	2015
CHO (g%)	233g/45%	329g/65%	317g/62%
Pro (g%)	77g/15%	76g/15%	77g/15%

Fat (g%)	92g/40%	46g/20%	54g/23%
Fiber (g)	22.8g	23.9g	25.2g
Chol (mg)	209mg	203mg	210mg
SFA (g)	28.2g	13.4g	14.8g
MUFA (g)	28.7g	13.9g	16.2g
PUFA (g)	28.0g	13.3g	16.1g
18:3 (g)	1.40g	0.85g	5.36g
20:5 (g)	0g	0g	0.46g
22:6 (g)	0.03g	.03g	0.99g
Omega 3 FA (g)	1.43g	0.88g	6.82g

Sample Menu 2000 Kcal) - Day 2

	Menu	High Fat	Low Fat	Low Fat + Omega 3
Breakfast	Wheaties	25g	35g	45g
	w/ Sugar	4g	6g	6g
	Orange	100g	150g	150g
	w/ Sugar	0	0	5g
	Orange Muffin	55g (High Fat)	50g (Low Fat)	50g (Low Fat, High Om-3)
	w/ Butter/Margarine	4g (Margarine)	5g (Butter)	3g (Butter)
	w/ Preserves	0	15g	0
	Milk-Skim/2%	200g (2%)	200g (Skim)	240g (Skim)
Lunch:	Chicken/Tuna Sandwich			
	Whole Wheat Bread	50g	65g	65g
	Lettuce/Tomato	20g/0	20g/50g	20g/50g
	Cheddar Cheese	15g	0	20g
	Miracle Whip-Reg/FF	10g (Reg)	15g (FF)	15g (FF)
	w/ Egg Yolk	0	4g	4g
	w/ Flax Oil	0	0	4g
	Chicken Breast/Tuna	60g (Chicken)	70g (Chicken)	70g (Tuna)
	Margarine	4g	0	0
	Carrots	60g	60g	60g
	Pineapple	100g	100g	100g
	w/ Sugar	0	5g	5g
Dinner:	Spaghetti with Meat Sauce			
	Ragu Lite	110g	150g	150g
	w/ Corn Oil	8g	0	0
	Spaghetti	80g	130g	150g
	Mushrooms	50g	50g	50g
	Lean Ground Beef	65g	60g	40g
	French Bread/White Bread	25g (White)	40g (French)	40g (French)
	w/ Butter	7g	5g	0
	Green Beans	100g	100g	100g
	Lettuce Salad	70g	75g	75g
	w/ Italian Dressing-Reg/FF	(Reg)	15g (FF)	15g (FF)
	w/ Fat Free Italian Dressing	0	15g	15g
	w/ Safflower Oil/Flax Oil	0	2g (Safflower)	3g (Flax)
	w/ Egg Yolk/Egg White	0	0	4.5g/15g
	Peaches	90g	100g	100g
	w/ Sugar	0	5g	5g
Snack	Blondies	50g (High Fat)	50g (Low Fat)	50g (Low Fat, High Om 3)
	Milk Chocolate Candy	15g	0	10g
	2% Milk	180g	0	0
	Gumdrops	0	35g	20g

Nutrient Composition (Calculated)

	2026	2006	2036
<i>Kcal</i>			
<i>CHO (g%)</i>	230g/45%	327g/65%	323g/62%
<i>Pro (g%)</i>	77g/15%	77g/15%	76g/15%
<i>Fat (g%)</i>	92g/40%	46g/20%	52g/23%
<i>Fiber (g)</i>	21.6g	27.2g	30.5g
<i>Chol (mg)</i>	204.1mg	201.3mg	213mg
<i>SFA (g)</i>	26.9g	12.4g	14.2g
<i>MUFA (g)</i>	30.4g	14.7g	14.4g
<i>PUFA (g)</i>	27.3g	12.99	14.2g
<i>18:3 (g)</i>	1.21g	.577g	6.786g
<i>20:5 (g)</i>	.006g	.008g	0.176g
<i>22:6 (g)</i>	.013g	.020g	.451g
<i>Omega 3 FA (g)</i>	1.23g	.605g	7.413g

Sample Menu 2000 Kcal) - Day 3

Menu	High Fat	Low Fat	Low Fat + Omega 3
Breakfast			
Pineapple Juice	120g	150g	140g
Wheat Chex w/ Sugar	30g 0	30g 4g	30g 4g
WW Bread/WW Bagel w/ Cream Cheese-Reg/Lite	50g (Bread) 30g (Reg) 10g (Diet Jelly)	60g (Bagel) 20g (Lite) 20g (Preserves)	60g (Bagel) 30g (Lite) 10g (Preserves)
Milk-Skim/2%	120g (2%)	200g (Skim)	200g (Skim)
Lunch:	Chicken/Salmon Pasta Salad		
Macaroni	80g	80g	80g
Chicken Breast/Salmon	80g (Chicken)	55g (Chicken)	65g (Salmon)
Green Onion	10g	10g	10g
Diced Celery	10g	10g	10g
Peas	15g	15g	15g
Garlic Powder/Salt/Pepper	Dash	Dash	Dash
Lemon Juice	2g	2g	2g
Mayonnaise	25g	9g	0
Fat Free Miracle Whip w/ Egg Yolk	0 0	20g 7g	30g 7g
Whole Wheat Bread w/ Butter/Flax Butter	25g 10g (Butter)	60g 4g (Butter)	30g 5g (Flax Butter)
Blueberries w/ Sugar	100g 0	100g 4g	100g 4g
Oatmeal Walnut Cookie	30g	30g	30g
Dinner:			
Beef Tenderloin	65g	60g	75g
Mashed Potatoes w/ Butter/Olive Oil	100g 5g/4g	140g 0	140g 0
Corn	80g	120g	120g
Whole Wheat Bread w/ Butter/Margarine	25g 9g (Butter)	30g 4g (Marg)	30g 0
Lettuce Salad w/ Ranch Dressing-Reg/FF	60g 15g (Reg)	60g 15g (FF)	60g 15g (FF)
w/ Corn Oil/Flaxseed Oil	0	3g (Corn)	3g (Flax)
Fruit Cocktail w/ Sugar	90g 0	100g 4g	100g 0
Snack	Brownie	60g (High Fat)	50g (LF, High Om 3)
	Raisins	0	30g

Nutrient Composition (Calculated)

Kcal	2010	2011	2009
CHO (g%)	232g	334g/65%	313g/61%

<i>Pro</i> (g/%)	75g	77g/15%	79g/15%
<i>Fat</i> (g/%)	92g	47g/20%	54g/24%
<i>Fiber</i> (g)	21.2g	27.6g	27.4g
<i>Chol</i> (mg)	241.3mg	218.7mg	231.8mg
<i>SFA</i> (g)	28.5g	13.4g	15.2g
<i>MUFA</i> (g)	28.6g	14.98g	16.1g
<i>PUFA</i> (g)	27.8g	12.8g	17.5g
<i>18:3</i> (g)	1.886g	1.172g	5.073g
<i>20:5</i> (g)	.008g	.006g	.449g
<i>22:6</i> (g)	.016g	.019g	.955g
<i>Omega 3 FA</i> (g)	1.91g	1.197g	6.472g

Sample Menu 2000 Kcal) - Day 4

	<i>Menu</i>	<i>High Fat</i>	<i>Low Fat</i>	<i>Low Fat + Omega 3</i>
Breakfast	Grape Juice	80g	100g	80g
	Rice Krispies	25g	30g	30g
	Whole Wheat English Muffin	40g	60g	60g
	w/ Butter/Margarine	6g (Butter)	3g (Butter)	3g (Butter)/3g (Marg)
	w/ Preserves	0	15g	15g
	Skim Milk	240g	200g	200g
Lunch:	Roast Beef Sandwich			
	White Bread	50g	50g	50g
	Roast Beef, Deli	40g	65g	65g
	Mayonnaise, Reg	22g	6g	0
	Fat Free Miracle Whip	0	10g	10g
	Flax Butter	0	0	4g
	American Cheese	30g	0	0
	Lettuce	20g	20g	20g
	Tomato	50g	50g	50g
	Fritos/Pretzels	30g (Fritos)	25g (Pretzels)	25g (Pretzels)
	Peaches	90g	100g	100g
Dinner:	Blondies	0	55g (Low Fat)	55g (Low Fat)
	Fish/Salmon Cakes	180g (Fish)	200g (LF Fish)	200g (Salmon)
	w/ Sour Cream Sauce-Reg/Lite	25g (Reg)	20g (Lite)	20g (Lite)
	w/ Dill/Salt/Pepper/Lemon	Dash	Dash	Dash
	Brown Rice	110g	120g	100g
	w/ Butter	3g	0	0
	Carrots	100g	100g	100g
	Lettuce Salad	70g	70g	70g
	w/ Egg White	25g	0	0
	w/ French Dressing-Low Cal/FF	15g (Low Cal)	15g (FF)	15g (FF)
	w/ Corn Oil/ Flaxseed Oil	8g (Corn)	3g (Corn)	6g (Flax)
Snack	Whole Wheat Bread	25g	60g	60g
	w/ Butter/Flax Butter	5g (Butter)	5g (Butter)	3g (Flax Butter)
	Pears	80g	120g	120g

Nutrient Composition (Calculated)

Kcal	2003	2013	2041
CHO (g%)	229g/45%	330g/65%	319g/62%
Pro (g%)	73g/15%	73g/15%	73g/14%

Fat (g/%)	91g/40%	46g/20%	54g/24%
Fiber (g)	17.7g	23.6g	23.2g
Chol (mg)	240.96mg	196.6mg	209.6mg
SFA (g)	28.5g	13.4g	14.3g
MUFA (g)	27.97g	14.9g	17.5g
PUFA (g)	28.7g	13.97g	18.4g
18:3 (g)	2.429g	.864g	5.749g
20:5 (g)	.002g	.002g	.338g
22:6 (g)	.008g	.008g	0.72
Omega 3 FA (g)	2.432g	.874g	6.807g

Sample Menu 2000 Kcal) - Day 5

	<i>Menu</i>	<i>High Fat</i>	<i>Low Fat</i>	<i>Low Fat + Omega 3</i>
Breakfast	Orange Juice	120g	220g	220g
	Shredded Wheat	25g	35g	35g
	w/ Sugar	0	6g	6g
	Whole Wheat Bagel	60g	60g	60g
	w/ Cream Cheese-Reg/FF	30g (Reg)	30g (FF)	30g (FF)
	w/ Preserves	0	20g	20g
	w/ Margarine	5g	0	0
Lunch:	Skim Milk	120g	200g	140g
	Chicken/Salmon Salad Sandwich			
	Cracked Wheat Bread	50g	60g	60g
	Chicken Breast/Salmon	60g (Chicken)	45g (Chicken) 7g (Reg)/10g (FF)	60g (Salmon)
	Miracle Whip-Reg/FF	30g (Reg)		10g (FF)
	Egg Yolk/Flax Oil	0	7g (Yolk)	7g (Yolk)/4g (Oil)
	Lettuce Leaf	20g	20g	20g
	Carrot/Cucumber	60g/40g	60g/40g	60g/40g
	Raspberries	80g	110g	110g
Dinner:	w/ Sugar	0	6g	6g
	Brownie	50g (High Fat)	40g (Low Fat)	40g (Low Fat)
	Meatloaf	100g	80g	80g
	w/ Fat Free Gravy	40g	40g	40g
	w/ Safflower Oil/Flax Oil	7g (Safflower)	3g (Safflower)	3g (Flax)
	Mashed Potato	100g	140g	140g
	Green Beans	100g	100g	100g
	Spinach Salad	70g	70g	70g
	w/ Fat free Ranch	15g	15g	15g
	w/ Safflower Oil/Flax Oil	7g (Safflower)	4g (Safflower)	3g (Flax)
Snack	Whole Wheat Roll	25g	45g	30g
	w/ Butter	8g	0	0
	Pineapple	80g	120g	120g

Nutrient Composition (Calculated)

Kcal	1979	2009	2000
CHO (g%)	232g/45.5%	332g/64%	320g/62%
Pro (g%)	76g/15%	80g/15%	77g/15%
Fat (g%)	89g/39.5%	48g/21%	54g/23%
Fiber (g)	32.7g	40.6g	39.5g
Chol (mg)	198.7mg	198.4mg	198.1mg

SFA (g)	27.3g	13.5g	14.8g
MUFA (g)	27.4g	15.7g	18.0g
PUFA (g)	27.7g	14.3g	15.8g
18:3 (g)	1.327g	.778g	5.824g
20:5 (g)	.006g	.005g	.415g
22:6 (g)	.013g	.018g	.883g
Omega 3 FA (g)	1.346g	.963g	7.122g